Hi Dr. Roethig and Denise:

Thank you again for the information below. As we are reviewing the protocol for the Total Exposure Program and determining our strategy, I was wondering if you had tentative timelines for the following:

Investigator Meeting
Enroll first subject
Enroll last subject
Submit last CRF
Lock database
Final study report

This information will be very helpful as it will allow us to evaluate the resources needed for the study.

I look forward to hearing from you.

Best regards,
Doug

Doug Fulling, MHA
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Global Clinical Research
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Doug.Fulling@mdsps.com

Hans-Juergen.Roethig@pmusa.com on 07/29/2002 05:49:42 PM

To: Doug Fulling/Irvine/MDSPS@MDS
cc:
Subject: TES proposal

Dear Dough,

I am sending you the final protocol of the "Total Exposure Study", which will involve 4000 smokers (representative of the US smoking population) and 1000 comparable non-smokers. Further details you will find in the sampling plan. I have also added the summary of the statistical analysis plan.

I would appreciate if you could give me a price for this study including:

Recruitment of 30 - 40 sites across the US,
Management of these sites including investigators meeting and all shipments of samples,
Monitoring of the sites,
Clinical laboratory work,
Data management, stats and report, (please be aware that the bioanalytical work will be done at Covance and MDS in Lincoln and data will be transferred in EXCEL),

Missing subject number
Subject number format
Duplicate subject number
Duplicate subject number by investigator
Subject number range by investigator
Missing randomization number
Randomization number format
Duplicate randomization number
Missing results
Pending tests
Outstanding queries

Global data validation procedures are divided into two categories: study non-specific, and study specific, covering the backbone of laboratory data interchange (panel profiles, range checks, analyte mapping). Study specific procedures are designed based on study requirements and may include specific range checks, specific alerts, and specific conditional validation routines.
All procedures are designed following the below principles:
a. Data validation must be real-time or as close to real time as possible.
b. Data validation must be close to the source of data.
c. Data validation output must be human readable.
Frequency of data validation is linked to the frequency of data uploads and can vary from real-time to monthly."

Hans-Juergen.Roethig@pmusa.com on 08/13/2002 01:14:36 PM

To: Doug Fulling/Irvine/MDSPS@MDS
cc:
Subject: RE: TES proposal

Hi Dough,
thank you again for coming and visiting us here in Richmond! You and Tony gave us a good impression of MDSPS's phase II/III services. Do you have an idea, when we could get your revised proposal? Before we make a final decision we would also like to meet with the key team members from MDSPS.

Looking forward to your answer
Best regards
Hans

-----Original Message-----

From: **Doug.Fulling@mdsps.com [mailto:Doug.Fulling@mdsps.com]**
Sent: Thursday, August 01, 2002 8:03 AM
To: Hans-Juergen.Roethig@pmusa.com; Denise.T.Mawyer@pmusa.com
Cc: rae@mdsharris.com
Subject: Re: TES proposal

Hi Hans,

It was a pleasure meeting the team and we look forward to learning more about your initiatives for 2003. I am in the King of Prussia office today and working with Tony on our revised proposal. As we are working on the proposal, we wanted to clarify a couple of points:

- We are assuming the eCRF system utilized will be cleaning and capturing the data
- We are assuming that we will be receiving lab data electronically
- We are assuming that we will be receiving the questionnaire file with scanned data

Please let me know if these assumptions are correct and will be able to turn around a budget estimate to you quickly. Also, let me know if there are any line items you would like us to remove from our previous proposal, ex: coding.

With our assumptions and the information you shared with us, we feel we can significantly reduce our original budget estimate.

On another note, per your question about Central Labs and data validation, please find the MDS Pharma Services' perspective below. If you have further questions, I would be happy to put you in touch with a representative from Central Labs.

Best regards,
Doug

Please find the following explanation of our data cleaning process for Central Lab. This process along with the trial size, complexity, number of testing locations, data interchange volume, study testing profile and required resources to guarantee data quality are included as part of our charge for electronic data transfers. Please note that we only invoice clients for actual data transfers.

"Data cleaning at MDS Pharma Services Central Lab is a two-stage process.

First stage is carried out during data acquisition and covers the following:

. Completeness of demographic information and sample reconciliation.
. Legibility of source documentation and appropriateness to study protocol.
. Data formats and range checks including dates, times, fasting status and study specific subject population.

Data query forms (DQF) are issued to clarify discrepancies encountered during data acquisition. DQFs are faxed and followed through with a phone call within the agreed sponsor approved period. Should discrepancies remain unresolved, they are raised to the attention of sponsor or local monitor.
All data entry activities are subject to 100 % independent audit carried out within 24 hours of the activity. Documentation of the audit and its results are part of departmental performance management and archived with source documents.
The second stage of data cleaning is carried out prior to any electronic file transfer (EFT) and it is designed to confirm the quality of transferred data, cover complex logic checks, and assure error free loading into the remote database. Exhaustive checks performed include but are not limited to the list below. Additional checks are developed as required per protocol specifications.

Missing center numbers
Duplicate center numbers
Duplicate investigators
Missing collection time
Missing collection date